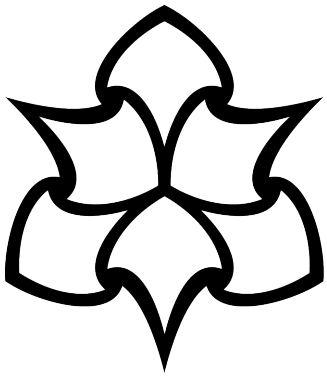

What is known from the existing literature about men living with HIV, erectile dysfunction and role of HIV nurses: a scoping review

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Introduction

This article reviews the current literature regarding HIV and erectile dysfunction. The article will explore why erectile dysfunction is more common in men who are HIV positive as appose to men who do not have HIV. A detailed review of the current literature in the form of a scoping review was undertaken to explore the current links between HIV and erectile dysfunction. Only literature that has meet the inclusion and exclusion criteria will be included in this article. Themes that emerge from the literature will be grouped together in order for recommendations to be drawn.

Why was the review performed?

The initial idea behind this review emerged from a lack of understanding by the first author with respect to this field of nursing and anecdotal evidence from colleagues that nurses may not have the knowledge, or be managing erectile dysfunction in practice, and instead refer such patients to the medical team for care and management. This article forms part of the first author's MSc dissertation.

Why is this an issue in clinical practice?

With increasing numbers of people living with HIV, and as HIV becomes a long-term condition, the role of the nurse within this disease area is changing. There is a growing need to find ways to support nurses within clinical practice to manage erectile dysfunction.

What is erectile dysfunction and how much of an issue is it in practice?

Erectile dysfunction (ED) is typically defined as the inability to achieve or maintain an erection for satisfactory sexual activity [1], with an incident rate in the general population living without HIV ranging from 26 cases per 1000 men in the USA [2] to 39 per 1000 cases in Finland [3,4] and finally 66 cases per 1000 in Brazil [5]. Incidence rates increased across all of these studies with age. Men living with HIV (MLWH) are statistically more likely to suffer from ED than men without HIV [6]. Cases of sexual dysfunction linked to HIV have been reported from just after the pandemic began [7].

Methodology: reviewing the literature

The literature was reviewed using the following search terms: human immunodeficiency virus; HIV; acquired immunodeficiency syndrome; AIDS; erectile dysfunction; sexual dysfunction; management; and nursing/nurse. Numerous databases were searched including CINAHL Complete, Academic Search Complete, Medline and PsychINFO. The Cochrane Library was also searched and one suitable article was located and although it did not prove relevant in the field of nursing or medical management, it did provide detailed statistics about prevalence of ED in people living with HIV (PLWH).

Manual searching of journals including *HIV Nursing*, *HIV Medicine*, *AIDS Care*, *HIV & AIDS Review*, *Southern African Journal of HIV Medicine*, *African Journal of AIDS Research*, *AIDS and Behavior*, *AIDS Patients Care and STDs*, *AIDS Research and Therapy* and *AIDS Research and Treatment*, allowed for additional articles to be added to the review. It is important to remember that key journal searches are useful to add further articles to the review [8].

A search of the academic textbooks available was also undertaken to identify texts that may be useful for nurses in their education on HIV and ED. Finally, a search of the grey literature was performed to locate relevant data that may be of benefit and not located during traditional searching. The advantage of searching the grey literature is to broaden the scope to more appropriate studies, therefore, providing a complete review of the relevant literature [9]. Google Scholar can be useful in this situation and may add additional resources to the literature search. Additional articles can be added to the review from back-chaining and utilising the feature in Google Scholar entitled 'cited by'. This function allows newly-published data that has used previously identified studies to be added to a review. This is often referred to as 'berry picking' and can include reviewing an author's other publications [10]. Finally, colleagues and specialists in the field from the National HIV Nursing Association were approached about 'HIV and erectile dysfunction'

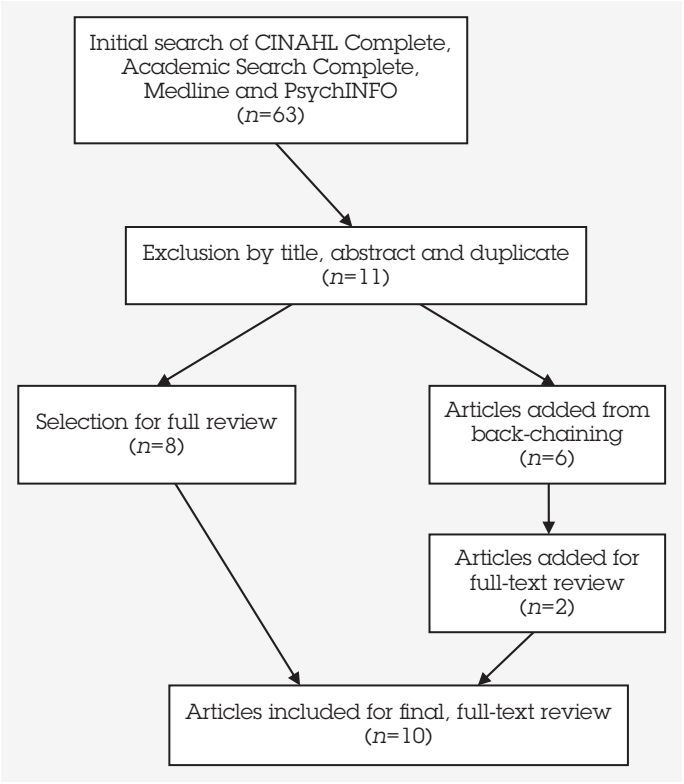

Figure 1: *Search strategy and findings.*

to further add any additional resources or advice to the study. This process can generate additional sources of information and provide additional insight in to the chosen topic [11].

The literature review process is a valuable stage in the research process as it shows what studies have previously been undertaken, it is a way of learning about existing theories and ideas, allowing for new research approaches to develop from the learning and finally justifies the research project [12]. A scoping review was decided upon due to the complexity of words used within the chosen topic. Previous studies have approached their research in this way [13], and such a review allows for a broader range of literature to be searched [14]. Furthermore, it aims for breadth and comprehensiveness rather than for depth in the research [8].

The process for undertaking a scoping review can be divided in to five stages [8]:

Stage 1: Identifying the research question
Stage 2: Identifying relevant studies
Stage 3: Study selection
Stage 4: Charting the data
Stage 5: Collating, summarising and reporting the results

The first aim, and fundamentally important part, of the study is to identify a suitable research question for the scoping review. The question for the purpose of this scoping review was:

> *What is known from the existing literature about MLWH and erectile dysfunction and the role the HIV nurse plays?*

The search strategy loosely mirrored a piece of research published in the *Journal of Advanced Nursing* and this article follows a logical and constructive way of searching the literature [15]. Figure 1 describes the search strategy and findings. Initial searching of CINAHL Complete, Academic Search Complete, Medline and PsychINFO using key words discussed earlier found 63 results. Once duplicates had been removed from an initial search of 63, 38 articles were left. The 38 articles had their abstracts reviewed and selected if they met the inclusion criteria, which were that the articles must:

- Report, investigate or contain information relevant to the topic
- Be published 2005–2015
- Be English language studies only
- Be studies dedicated to men, HIV and ED

From this review, 11 articles were selected, however, only eight were accepted for final inclusion in the review, again following the inclusion criteria. Back-chaining allowed another six papers to be identified for review and two of these were carried forward into the study. In total 10 papers were included for the final review (Table 1). One additional study, found in the Cochrane Library had already been included in the study. Grey searching and utilising Google Scholar did not locate any additional suitable articles, nor did manually searching the suggested specific journals mentioned earlier.

Using recent sources of information that have been published in the last 10 years allows for current or fairly recent information to be used within the study and is widely recommended in the research. As a result of this process 10 articles in total were selected for review and were explored.

Results

Table 1 shows the studies and demonstrates that they are from an international arena with work published pan-Europe (including the UK), in Belgium, Italy, Mexico, Spain, Switzerland and the USA. Sample size varies from 90 to 4064 MLWH, and two of the studies used a comparison with men not living with HIV. All of the articles were published in peer-reviewed journals and were published 2006–2014. All used a quantitative approach, mainly using the International Index of Erectile Dysfunction questionnaire or an adapted version. Most of the studies looked at heterosexual men or men who have sex with men (MSM), although one study was dedicated just to MSM.

A number of key topics were highlighted from the review that show ED in MLWH is more common and, furthermore, the question of why is not simple to answer. Cholesterol levels; a person's mental health status; their CD4 count at diagnosis and present CD4 count; ART and the length of time a person has been

Table 1: Articles included for final review and findings

Number	Author, publication year	Country	Methodology	Sample size	Ethical considerations	Data collection	Key findings
1	Romero-Velez *et al.* 2014	Mexico	Cross-sectional study	109 men	Approved by local ethics committee	Self-completion of International Index of Erectile Dysfunction Questionnaire, which if indicated ED led to case note reviews of possibilities	64% prevalence rate of ED noted in MLWH Dyslipidaemia notes as only significant variable that may increase likelihood of ED
2	Crum-Cianflone *et al.* 2007	USA	Mixed method study using both quantitative and qualitative data	300 men	Unclear	Self-completion of International Index of Erectile Dysfunction Questionnaire, physical exam and laboratory testing for testosterone levels	61.4% prevalence rate of ED noted in MLWH Depression and age linked to reasons why MLWH may have ED No significant association between HIV HAART and ED
3	Ende *et al.* 2006	USA	Cross-sectional, mixed method review	118	Ethics approved	Self-completion of International Index of Erectile Dysfunction Questionnaire, medical note review and laboratory testing for testosterone levels	74% prevalence rate of 'mild' ED noted in MLWH Treatment rate is 11% so likely under treatment of ED No clear reason why ED affects men
4	Zona *et al.* 2012	Italy	Cross-sectional, observational and controlled study of men with and without HIV	441 men with HIV and 71 men without HIV	Signed and informed consent took place	Self-completion of International Index of Erectile Dysfunction Questionnaire, medical note review and laboratory testing for testosterone levels	Increased levels of ED with age in both groups of men, however ED appears to start earlier in life for MHIV
5	De Ryck *et al.* 2013	Belgium	Cross-sectional and observational study	244 MLWH	Ethical approval noted	Self-completion of International Index of Erectile Dysfunction Questionnaire and further blood analysis	61.9% of men reported ED issues HIV-related parameters, or any of the individual cardiovascular risk-related parameters were statistically significantly associated with ED
6	Perez *et al.* 2013	Spain	Observational study	158 MLWH	Ethical approval noted	Self-completion of International Index of Erectile Dysfunction Questionnaire and an anxiety and depression survey	67.1% of men reported ED issues Depression and anxiety clearly linked to ED
7	Moreno-Perez *et al.* 2010	Spain	Cross-sectional and observational study	90 MLWH	Ethical approval noted	Self-completion of International Index of Erectile Dysfunction Questionnaire and case note reviews	53.4% of men reported ED Protease inhibitors linked to ED
8	Wang *et al* 2013	Switzerland	Cross-sectional study	4064 MLWH answered questions on ED	Informed consent obtained	One question on frequency of ED and current data already held about HIV drug treatment	11% of men reported ED often No connection between HAART drug treatment and ED
9	Shindel *et al.* 2011	International	Cross-sectional	110 MLWH 1125 without HIV	Ethics approved	Self-completion of International Index of Erectile Dysfunction Questionnaire and other medical questions	There was a significant trend toward greater prevalence of ED in men with progressive HIV infection 40–59 years of age
10	Asboe *et al.* 2007	Europe	Cross-sectional	711 men with HIV	Ethical approval obtained	Part completed in clinic and part completed at home	32.9% reported ED No association between HAART and ED

ED: erectile dysfunction; HAART: highly activated antiretroviral therapy; MLWH: men living with HIV.

on treatment; the type of sexual activity; and finally; testosterone levels all play roles and may influence whether a person is more likely to suffer from ED. The studies themselves contradict each other and subsequent studies have been unable to replicate earlier studies. The cause of ED is still poorly understood in MLWH and this review highlights that further research is needed in the area to try to answer such a question. Conclusively, health professionals need to screen patients for ED as it is highlighted in several of the studies that a higher rate of ED is noted, yet, patients have not been offered appropriate treatment (see later).

Studies that connect HIV with ED demonstrated the complexity and lack of understanding about what is more likely to cause ED in MLWH. Each study demonstrated an increase or high prevalence of ED ranging from 32.9% [16] to 74% reporting mild symptoms [4].

Dyslipidaemia

Dyslipidaemia (raised cholesterol levels) was associated in one study as the only potential link to ED for MLWH however the article highlights that this needs to be studied further [17]. Although this study acknowledges the role medications (particularly statins – cholesterol lowering drugs) play, they were not evaluated with regards to their effects on ED or how they may improve ED. This may alter the findings of this study specifically as the conclusions highlight that higher levels of cholesterol are associated with ED. It was the only study to highlight a connection between HIV, ED and dyslipidaemia. However, other studies of men without HIV have linked raised cholesterol with ED, even when men are taking statins [18,19], therefore, showing there would appear to be a clear link, however, this may not be the reason why MLWH have a higher incidence of ED.

Mental health

Four of the studies linked ED with some aspect of mental health. Interestingly, one study showed in its statistical analysis of a large multivariable study of 711 MLWH, an association between antidepressants/other psychotropic medication use and ED [16]. However, this study failed to show or provide reason why this may be; and so, as noted in their limitations, this may be a spurious association (due to the large number of variables).

In the Swiss cohort study, a connection between ED and depression was highlighted showing the role that psychiatric and psychosocial factors play in healthy sexual function [20]. The study did not explore further or provide reasons why this may be the case, therefore, additional analysis is required to investigate this. The authors self-report multiple limitations in the study, mainly that only one question was asked about ED and that the validated, International Index of Erectile Dysfunction Questionnaire was not used.

In a study of 158 men, a significant link was found between anxiety and depression with ED and how feelings of guilt, principally about how the men may have acquired their HIV status, may be a psychological factor that is inadvertently affecting sexual function [21]. Furthermore, this psychological factor may go on to explain higher rates of sexual dysfunction in MSM, which has been reported in other studies [22,23].

Crum-Cianflone *et al.* used a self-completed questionnaire from 300 MLWH [24]. Participants completed the International Index of Erectile Dysfunction Questionaire and the Beck Depression Inventory, which is widely used to diagnose depression and anxiety [25]. The study showed 40% of men with ED were depressed compared to 12% of men who did not have ED. Strikingly, the authors note that each condition, namely, ED and depression, may exacerbate each other and it is unclear in that case which one is the primary problem. Early diagnosis and treatment of depression for MLWH may be beneficial in improving or preventing ED, although, more research is needed to support this.

CD4 count

Crum-Cianflone *et al.* [24] go on to report how the CD4 count is predictive of ED. The study clearly showed a lower nadir CD4 count (the level of the immune system at HIV diagnosis) in patients is more likely to mean they may have ED. Put simply, this means the sooner a patient is diagnosed with HIV, the higher the CD4 count will be, meaning they may be less likely to develop ED, this reinforces the argument for early diagnosis and treatment. Commencing treatment early and reducing the likelihood of the CD4 count dropping by starting ART may be beneficial in preventing ED and starting treatment early has been shown to reduce AIDS-related problems [26]. In addition to this, low current CD4 count is predictive of ED, again supporting early commencement of ART.

Ende *et al.* [4] reported higher rates of ED in their study (n=118). Their findings did not demonstrate any correlation between current CD4 count and whether the men were likely to have ED contradicting Crum-Cianflone *et al.'s* study. Interestingly, Ende *et al.* did not demonstrate any correlation between any of the study's variables, which included age, whether currently on ART, opportunistic infections or median testosterone levels; this may have been due to a lack of 'power' from the relatively small sample size.

Ende *et al*'s study identified that some men were undertreated for ED with only 11% out of the 74% of men in the study who reported ED, being treated. They rationalised this by discussing that treating ED

with phosphodiesterase type 5 inhibitor ([PDE5] drugs to help achieve an erection) may lead to risky sexual behaviour. This may prevent the clinical team prescribing these medications to avoid the onward transmission of HIV. This is supported by another study of 413 participants that suggested that PDE5 drugs prescribed to MLWH may lead to 'potentially transmitting sexual risk behavior' [27]. However, with the advances in ART treatment and, furthermore, the fact that HIV treatment lowers HIV viraemia (amount of HIV in the body) this will make an individual with HIV extremely unlikely to transmit HIV, if they are complying with treatment regimens [28]. This should, therefore, no longer be an issue. Interestingly, Ende *et al.* do support the prescribing of PDE5 inhibitors but only after advice on; safe sex, condom use, sexually transmitted infections and education about the risks.

Underuse of PDE5 inhibitors (such as Cialis and Viagra)

Moreno-Pérez *et al.* [29], discuss how underused PDE5 inhibitors are in their study of 90 patients, of which 47 reported suffering with ED. Of these only 11 had actually tried PDE5 inhibitors as a treatment option but remarkably nine of these (81%) reported that they had been effective, showing the lack of use in clinical practice when the drug appears to be helping. Despite the lack of randomised control trials of MLWH and the efficacy of PDE5 inhibitors it is widely accepted as a first line therapy to treat ED [29].

Unsurprisingly, De Ryck *et al.* discuss that MLWH and ED are more likely to use PDE5 inhibitors than men without ED; in spite of this only 7% of men reported using this medication either most times or almost always when engaging in sexual activity [30]. This again highlights the under use of PDE5 inhibitors by MLWH. De Ryck *et al.* goes on to discuss how screening of all MLWH should take place to identify ED. Clinical teams need to be pro-active rather than reactive in this area. Once identified, PDE5 inhibitors can be prescribed, but, in the interests of public safety recommending it should be accompanied by safer sex counselling [30].

HIV Treatment

The use of HIV ART has long been associated with ED, particularly one group of ART, namely the protease inhibiting (PI) drugs [31]. Only one study out of the ten used in this scoping review, highlighted that PIs are linked to ED [29], and although Moreno-Pérez *et al.*'s study does highlight that a PI may be associated with an increased likelihood of ED, it is a small study of 90 patients of whom only 39 were actually taking a PI; their study acknowledges the small scale of the sample within its limitations.

Asboe *et al.* within their study, note that the use of ART per se does not influence ED but the length of time someone is on treatment does [16]. It is significant when someone has been on treatment for longer than 81 months, but this could not be attributed to PIs alone and instead was considered to be related to ART in general. Interestingly, within their study they report that some participants stopped or switched ART due to ED. Most who did, came off a PI-based regime and some did report improvement, the authors stress that they cannot assume it was the ART that was responsible for ED. In contrast, Romero-Velex *et al.* note there is no correlation between any groups of drugs or the length of time that the person takes them for and ED [17].

Wang *et al.* report no correlation between ED and any group of ART although they do mention two specific drugs out of 25 (zalcitabine and enfuvirtide) that may be slightly more likely to be correlated with ED, although neither of them are used frequently today [20]. Crum-Cianflone *et al.* report no correlation between ED and ART. Their study looked specifically at groups of drugs and individual drugs, and no significant association was seen [24]. It was first reported that PIs had a link to ED but it is clear that this has not been clearly identified since to be significant [32].

Sexual activity

Romero-Velex *et al.* recognise in terms of prevalence of ED that there is no difference between MSM living with HIV, or heterosexual men living with HIV [17]. Zona *et al.* also reported no difference between MSM and heterosexual men but suggested that the International Index of Erection Function probably fails when comparing results from heterosexual men and MSM [33]. The problem they suggested is that MSM require a higher penile rigidity for anal penetration and therefore suggest that this group of men would report worse ED symptoms. By contrast, Asboe *et al.* report more heterosexual men are likely to have ED than homosexual men [16].

Shindel *et al.* compare men who have sex with men living with HIV, with men who have sex with men without HIV. They reported a higher incidence of ED in patients with progressive HIV (advanced HIV status) and men that were aged above 40 years of age [34]. They hypothesised that ED occurs around 10–15 years sooner in men with HIV than without HIV. In their study they did not assess whether ART impacts ED and this is highlighted as a limitation of the study.

Testosterone levels

Zona *et al.* reported that hypogonadism (low testosterone levels) is to be linked to ED in MLWH [33]. Erectile dysfunction has been linked to hypogonadism as testosterone is required for normal erection, although, ED has been seen in men with normal testosterone levels too [35]. Furthermore, in the pre-ART availability era hypogonadism was seen frequently

[7], however, since the introduction of ART, levels of hypogonadism appear to be reducing [36]. Although, Crum-Cianflone *et al.* show no correlation between low testosterone levels, and current, past or cumulative use of ART [24], in contrast, De Ryck *et al.* present 18 out of 49 men in their study who had their testosterone levels checked and were shown to be testosterone deficient [30]. Furthermore, they suggest routine screening of ED using a tool such as the International Index of Erection Function and subsequently testosterone level testing. If low testosterone is detected it would be beneficial to consider testosterone replacement alongside PDE5 inhibitors.

Discussion

The differences identified within in all of the studies highlights that ED in MLWH are a multifaceted issue with no clear answers emerging. The variances seen can be explained by the different study designs, study populations and the changing tools used to evaluate ED. Cholesterol levels; a person's mental health status; their CD4 count at diagnosis and present CD4 count; ART and the length of time a person has been on treatment; type of sexual activity; and finally testosterone levels all play roles that may influence whether a person is more likely to suffer from ED. Of note none of the studies reported the role of the nurse in the management of ED but some of the studies did note that 'healthcare professionals' involved in HIV care should screen patients for ED. From the evidence presented above it is clear that screening should be carried out within clinical practice, however from the literature reviewed it suggested that it is unclear as to whether this is happening and further research is required to establish this and clarify the current situation within clinical practice.

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Renal disorders and HIV: answers to the self-assessment quiz

1. The correct answer is **d** i.e. the kidneys receive approximately 20% of cardiac output
2. The correct answer is **b** i.e. filtration is the main function of the glomerulus
3. The equation takes into account the serum creatinine, age, ethnicity and gender
4. Answers **a** and **c** are correct
5. *All* of the answers are possible causes of glomerulonephritis
6. An eGFR<15 is found in stage 5 i.e. end-stage renal disease
7. The correct answer is the blood urea nitrogen result or BUN
8. Answer **b** is correct
9. The statement is 'true'
10. You could answer any three of the following: excessive use of NSAIDs, recreational drug use, uncontrolled hypertension, uncontrolled diabetes, cigarette smoking, dehydration or high protein diet.
11. Answers **a, b, d** are correct. The kidneys are usually enlarged on ultrasound.
12. Answer **d** is the only correct criteria according to current British Transplantation Society guidelines